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PATENT

## REMARKS

Claims 1-3, 5, 6, 12-24, and 47 were pending in the present application. Claims 1, 5, 12, 22, and 47 have been amended herein. No new matter has been added. Upon entry of the present amendment, claims 1-3, 5, 6, 12-24, and 47 will remain pending. Because the amendments to the claims remove issues for appeal (*i.e.*, indefiniteness), Applicants respectfully request that they be entered into the record. See, M.P.E.P. §714.12.

**I. The Claimed Invention Is Novel**

Claims 17-20 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Gillaspy et al., GenEmbl Accession No. U39059 (18 November 1996) (hereinafter, the "Gillaspy reference"). The Final Rejection asserts that the Gillaspy reference reports a DNA sequence consisting of 60 contiguous nucleotides of SEQ ID NO:1 that are not selected from nucleotides encoding amino acids 70 to 136. Applicants traverse the rejection and respectfully request reconsideration because the Gillaspy reference does not teach every feature recited in claims 17-20.

A sequence alignment of the Gillaspy sequence and SEQ ID NO:1 shows only that the two sequences possess 52 contiguous adenosines in common in the poly A tail and 8 other bases in common. The Gillaspy sequence, however, does not represent a nucleic acid probe because it has only limited GC content and does not appear likely to act as a probe at a reasonable stringency; nor would it represent a suitable primer because it does not appear likely to bind to the target at the temperatures normally used for specific amplification. Further, one skilled in the art would be very unlikely to select a probe that contains a sequence that is quite clearly not in any way specific to a particular sequence. Thus, although the Gillaspy sequence is a DNA sequence, it does not amount to a probe or primer.

The Final Rejection asserts that Applicants are arguing features that are not recited in the claim. To the contrary, Applicants are not reciting "a nucleic acid molecule" in the claim; rather, Applicants recite a "probe or primer" in the claim. The terms "probe" and "primer" actually mean something to one skilled in the art and are distinguishable as a subtype of a nucleic acid molecule. Probes and primers have inherent features such as those discussed above which

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render them useful as probes or primers. Indeed, one skilled in the art would be very unlikely to select a probe that contains a 52-base polyA sequence that would quite clearly not be specific to a plant DP sequences. Thus, although the Gillaspy reference reports a nucleic acid molecule, the nucleic acid molecule is not a probe or primer.

Thus, the Gillaspy reference does not teach every feature recited in claims 17-20. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

## **II. The Claimed Invention Is Useful**

Claims 1-3, 5, 6, 12-24, and 47 are rejected under 35 U.S.C. §101 as allegedly failing to be supported by either a specific, substantial, or a well-established utility. Claims 1-3, 5, 6, 12-24, and 47 are also rejected under 35 U.S.C. §112 as because one skilled in the art would allegedly not know how to use the claimed invention. The Final Rejection asserts that Applicants have not established a specific use for the claimed DNA sequences, and thus, the claimed DNA sequences have no real-world use. Applicants traverse the rejection and respectfully request reconsideration thereof because the claims are supported by specific, substantial, and credible utilities, and thus one skilled in the art would know how to use the claimed invention.

The Final Rejection asserts that the combination of sequence similarity and functional evidence in Applicants' specification does not establish a specific and substantial utility for the protein comprising SEQ ID NO:2. To the contrary, the protein comprising SEQ ID NO:2 is a previously undescribed member of the E2F dimerization partner (DP) proteins. This activity has been established through a combination of sequence similarity and functional evidence as presented in the application, for example, in Examples 1, 5, 6, 7, and 9 and Figures 2 and 3.

The Final Rejection asserts that partial homology between SEQ ID NO:2 and a protein of unknown function (referring to Figure 3) does not impute functional characteristics to SEQ ID NO:2. Applicants' specification, however, provides ample sequence similarity data to indicate that the protein comprising SEQ ID NO:2 is a plant DP protein. For instance, Example 1 in Applicants' specification teaches:

An amino acid homology study using the CLUSTALW routine (carried out on July 25,1999) with the available sequences of DP proteins from

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animal origin was carried out (Figure 2). Alignment of the TmDP with the animal DP sequences available in public databases revealed the existence of several conserved motifs, strongly suggesting that the TmDPcDNA clone encodes a protein belonging to the family. This together with its ability to interact with a plant E2F protein, indicates that the TmDPcDNA encodes a bona-fide plant DP protein. (emphasis added).

In addition, Example 9 in Applicants' specification teaches:

Characterisation of TmDP

**The idea that the isolated CDNA encodes a plant member of the DP family was reinforced by analysis of the amino acid homology and domain organization.**

TmDP exhibits an overall 29-33% amino acid similarity with human (Bandara et al., 1993; Girling et al., 1993; Krek et al., 1993) and X. laevis (Girling et al., 1994) DP-1 and DP-2 and a slightly smaller similarity (27%) with D. melanogaster DP (Dynlacht et al., 1994; Ohtani and Nevins, 1994). Amino acid alignment of plant and animal DP proteins indicates that it has a similar domain organization (Fig. 3B). The highest homology occurs within a 70 amino acid region (residues 64-143 in TmDP) which in animal DP proteins are important for DNA binding (Wu et al., 1996). This region includes a 10 amino acid stretch of fully conserved residues. Other amino acid blocks with a significant degree of homology contain the heptad repeats (residues 144-213 in TmDP), involved in heterodimerization with E2F (Wu et al., 1996; Zheng et al., 1999) and the domain conserved with E2F proteins (residues 214-240 in TmDP), a region which is similar to the E2F family members (Girling et al., 1993).

Experimental evidences of the heterodimerization properties of TmDP will be presented below in detail. Quite interestingly, TmDP lacks an acidic region which is present near the C-terminus of animal DP members, a domain whose functional significance has not been determined. Finally, the less conserved region corresponds to the N-terminal domain whose length and amino acid sequence is similar to that of animal DP members, in particular to the DP-2 group. Based on these homology studies, we conclude that TmDP presents a higher amino acid sequence similarity to animal DP-2. However, it is worth noting its smaller size and the absence of an acidic C-terminal domain as unique properties of TmDP.

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Thus, quite clearly, Applicants' studies of sequence data indicates that the protein comprising SEQ ID NO:2 is a plant DP protein.

The functional data presented in Applicants' specification also indicate that the protein comprising SEQ ID NO:2 is a plant DP protein. E2F transcription factor is a protein known to be involved in the transition of G1/S phases in the plant cell cycle. Typical DP proteins form stable heterodimers with E2F family members and can promote binding of E2F to DNA. The protein comprising SEQ ID NO:2 binds to and modulates the binding to DNA of the plant E2F transcription factor (see Examples 5-7).

The Final Rejection asserts that the binding of the protein comprising SEQ ID NO:2 to an E2F transcription factor protein and its stimulation of E2F binding to DNA does not establish a specific and substantial utility because it is not apparent how these properties have a real world use. It is not the properties per se, however, that provide the "real world use" of the protein. The combination of the sequence similarity data and the functional studies quite clearly establish that the protein comprising SEQ ID NO:2 is a plant DP protein. Plant DP proteins have quite many real world uses. Indeed, the description at page 4, line 14 to page 5, line 10 provides specific, substantial, and credible uses for modulation of these activities. Furthermore, these specific, substantial, and credible uses are supported by the teaching of PCT Publication WO0047614 (applicant Pioneer) which discusses even more specific, substantial, and credible uses for plants with modified expression of the DP proteins.

The Final Rejection states that since WO0047614 does not disclose SEQ ID NO:2, it does not establish a specific and substantial utility for SEQ ID NO:2. Applicants, however, have never asserted that WO0047614 discloses a protein comprising SEQ ID NO:2. Rather, WO0047614 teaches real world uses for DP proteins. Because the protein comprising SEQ ID NO:2 has been quite clearly established as a plant DP protein, and plant DP proteins have known specific, substantial, and credible utilities, the protein comprising SEQ ID NO:2 has at least one specific, substantial, and credible utility. Furthermore, DNA encoding such a protein also has at least one specific, substantial, and credible utility.

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Thus, the claimed DNA clearly has a useful, concrete and tangible use and, thus, is patentable subject matter. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §101/§112 be withdrawn.

**III. The Claimed Invention Is Supported by Ample Written Description**

Claims 1-3, 5, 6, 12, 13, 15, 22-24, and 47 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants traverse the rejection and respectfully request reconsideration because the specification provides ample written description supporting the claimed inventions.

As stated in the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1 'Written Description' Requirement":

Possession may be shown by actual reduction to practice, by a clear depiction of the invention in detailed drawings which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention, or by a written description of the invention describing sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention.

In accordance with these standards, Applicants have indeed, provided a sufficient written description of the claimed inventions. For example, claim 1 recites that the protein or peptide comprises at least one of the following structural features: a) the DNA binding domain, b) the heterodimerization domain, and c) the nuclear localization signal (i.e., a functional part thereof). These features are common to DP proteins, as outlined in Figure 2, and as described on page 12, lines 3-7, and as such are a recitation of features common to members of the genus, which features constitute a substantial portion of the genus. Claim 1, for example, also recites that the peptide or protein dimerizes with a plant E2F protein or peptide to increase or decrease E2F activity in the plant cell. Claim 1 also recites "or a sequence having at least 70% homology to either..." A description of a specific percent homology also provides an adequate written description. Thus, claims recite a proper combination of structure and function.

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The Final Rejection asserts that recitation of structure and function in the claim does not describe the claimed invention because the recited genus has not been described. In particular, the Final Rejection asserts that the one example provided in Applicants' specification does not constitute a representative number of species. Indeed, there are situations where a single specifically disclosed species is adequately supports a genus. For example, the MPEP §2163 states:

Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

The structural, homology, and functional features recited in Claim 1, for example, demonstrate Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Additional species are not warranted in the present situation because Applicants recite common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Further, the requirements of §112, first paragraph, regarding written description are met so long as the invention is described in the specification as broadly as it is claimed. *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971).

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, as allegedly failing to provide sufficient written description be withdrawn.

#### **IV. The Claimed Invention Is Sufficiently Enabled**

Claims 1-3, 5, 6, 12-24, and 47 are rejected under 35 U.S.C. §112, first paragraph as allegedly failing to provide an enabling disclosure. The Final Rejection mistakenly asserts that the enablement rejection is predicated in part on a failure to provide guidance with respect to the specific practice of particular techniques. The Office Action also appears to mandate a declaration regarding the availability of the deposit for pCLON33. Applicants traverse the rejection and respectfully request reconsideration because one skilled in the art would be able to practice the claimed invention without being required to perform undue experimentation.

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**PATENT****A. Claim 14**

The Examiner asserts that the plasmid pCLON33 "is required to practice the claimed invention." The Examiner also asserts that it does not appear that the specification provides a repeatable method for obtaining the plasmid. Although Applicants' specification provides ample basis for obtaining plasmid pCLON33, nonetheless, a nucleic acid encoding for a TmDP of sequence of SEQ ID NO:1 has been deposited on August 17th 1999 under the terms of the Budapest Treaty for the International Recognition of Microorganism Deposits for Patent Purposes of 28th in April 1977 at the Coleccion Espanola de Cultivos Tipo in plasmid pCLON33 under deposit number CECT 5195. The plasmid pCLON33 will be irrevocably and without restriction released to the public upon the issuance of the present application as a patent. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn

**B. Claims 12, 13, 15-24, and 47**

As a preliminary matter, claims 12, 13, 15-24, and 47 recite an "isolated, enriched, cell free and/or recombinant nucleic acid" (claims 12 and 13), a "nucleic acid probe" (claim 16), a "nucleic acid probe or primer" (claims 17 and 20), an "oligonucleotide probe" (claims 18 and 19), a "DNA which is antisense" (claim 21), a "nucleic acid" (claims 22 and 23), a "nucleic acid vector or construct" (claim 24), and a "nucleic acid encoding a DP peptide or protein fused to a sequence encoding a protein label" (claim 47). Thus, each of these claims recites compounds rather than methods of using compounds. No amount of undue experimentation is required to make any of the claimed compounds. Indeed, nucleic acid compounds are routinely made by those skilled in the art.

Applicants remind the Examiner that any use of the compounds recited in these claims is sufficient for purposes of enablement. For example, the claimed nucleic acid compounds can be used, for example, to either express a DP protein having SEQ ID NO:1, to detect nucleic acid sequences encoding a protein having SEQ ID NO:1, or can be used as a primer for amplifying a sequence encoding SEQ ID NO:1 (see, page 12, line 13 to page 16, line 12 of the specification). No amount of undue experimentation is required to use any of the claimed compounds, for

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example, to express a DP protein having SEQ ID NO:1, to detect nucleic acid sequences encoding a protein having SEQ ID NO:1, or as a primer for amplifying a sequence encoding SEQ ID NO:1.

The Final Rejection asserts that the rejection was predicated on Applicants' alleged failure to provide guidance on which specific nucleotide sequences to use as probes, the conditions for their use, and the specific targets that can be detected. The Final Rejection next asserts that such guidance is necessary because Gillespie, Vet. Microbiol., 1990, 24, 217-233 (hereinafter, the "Gillespie reference") purportedly sets forth that the conditions for using a sequence as a probe are unpredictable. Absent such guidance, the Final Rejection asserts that one skilled in the art would have to make the compounds and test them to determine which probe sequences are useful. Applicants disagree.

As set forth in the Office Action dated March 15, 2005, the Gillespie reference reports that specific hybridization between a DNA probe and its target sequence are affected by: 1) the concentration of probe and target molecules, 2) the length and sequence of the probe, 3) the hybridization temperature, and 4) the concentration of the salt and detergent present during hybridization. The fact that hybridization of a DNA probe to a target molecule is "affected" by any or all of these factors is wholly unsurprising. Indeed, these factors are simply the laws of physics that apply to hybridization of one entity to another entity. These factors, however, in no way, shape, or form amount to undue experimentation. Indeed, the use of DNA probes was routine in the art at the time of the Gillespie reference (1990), let alone as of 1999 (Applicants' earliest priority date). The literature is replete with references describing the use of DNA probes to nucleic acid molecules. Indeed, the general principles involved in the selection of DNA sequences for use as a probes is part of the common general knowledge of the ordinarily skilled molecular biologist. Further, it is routine practice in the art to optimize detection by varying temperature and salt concentration until satisfactory detection is achieved, and/or, if necessary, to use a selection of probes derived from the sequence. Since the sequence of SEQ NO:1, from which the probe sequence must be derived, is defined, the selection of probes does not involve examination of a myriad of possibilities, but is limited by the sequence from which the probe is derived (SEQ ID NO:1) and the selection of those areas of the sequence with the appropriate

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physical properties for use as a probe. These properties are well known in the art, consequently this does not represent an undue burden but is simply routine practice in the art to which the application relates.

In view of the forgoing, one skilled in the art would not be required to perform any amount of undue experimentation to make and use the compounds recited in claims 12, 13, 15-24, and 47. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

**C. Claims 1-3, 5, and 6**

As a preliminary matter claim 1 recites a method of controlling one or more of plant growth, gene expression, cellular DNA replication, cell cycle progression, differentiation and development by transforming the plant cell with a nucleic acid comprising a sequence encoding a peptide or protein that comprises SEQ ID NO:2, a functional part thereof, or a sequence having at least 70% homology to either. Claims 2, 3, 5, and 6 are dependent on claim 1.

The Final Rejection asserts that the rejection was predicated on Applicants' alleged failure to provide guidance with respect to which sequences to make and test, and with respect to which functional assays to apply to which sequences in order to discriminate between those sequences that function as desired and those that do not. Applicants disagree.

The claims recite that the proteins or peptides comprise at least one of the structural features a), b) and c) as described above. The specification teaches the function of these domains (see, for example, page 19, line 22 to page 21, line 16) and they are demonstrated to be present in other DP proteins. The specification teaches ample methods of verifying the activity of the proteins (see, for example, those of Examples 2, 4, 6, and 7). Therefore, there is no amount of experimentation identified in the Final Rejection that would be undue in order to practice the claimed invention.

The Office Action dated March 15, 2005 asserts that the invention is not enabled because "the effect of expressing in a cell a DP protein, alone or in combination with an E2F protein, is unpredictable, since different members of both the DP protein family and the E2F protein family vary with respect to their specific functions, and with respect to how they function

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when expressed independently and when coexpressed" (see, page 10 of the Office Action). Applicants disagree. The Office Action cites six references which purportedly supports the Examiner's position, only two of which relate to plant DP proteins.

The fact that DP proteins may have many different functions, particularly in non-plant cells, is wholly irrelevant in determining whether one skilled in the art can practice the claimed invention in plant cells without being required to perform undue experimentation. The various functions of DP proteins reported in the Hiebert, Dynlacht, Sawado, and Wu references are directed to non-plant cells. Applicants are unable to locate any portion of these references that teaches or suggests that the observations of different proteins in a different kingdom are what would also be expected in plants. Whether or not these functions are "predictable" is irrelevant when determining whether undue experimentation is required to carry out the claimed method in plant cells.

Magyar et al., FEBS Lett., 2000, 486, 79-87 (hereinafter, the "Magyar reference) does not teach or suggest that Applicants' claimed invention does not work or would require undue experimentation to work. Rather, as acknowledged in the Office Action dated March 15, 2005, the Magyar reference merely reports that *Arabidopsis thaliana* DP proteins do not group with animal DP families. Applicants are unable to understand any significance or relationship this plays in regard to Applicants' claimed invention. Again, nowhere does the Magyar reference teach or suggest that, because of the differences between *Arabidopsis thaliana* DP proteins and animal DP proteins, Applicants' claimed invention (which makes use of wheat DP proteins) would not function in plants, or would require undue experimentation to work in plants.

Mariconti et al., J. Biol. Chem., 2002, 277, 9911-9919 (hereinafter, the "Mariconti reference) also does not teach or suggest that Applicants' claimed invention does not work or would require undue experimentation to work. Rather, the Mariconti reference reports the existence of another group of E2F proteins in *Arabidopsis thaliana* which appear to lack the ability to bind to DP proteins, in addition to the group of E2F proteins that can bind to DP proteins. The Mariconti reference speculates that this additional group of E2F proteins can compete with the "wild-type" E2F proteins. Again, Applicants are unable to understand any significance or relationship this plays in regard to Applicants' claimed invention. Nowhere does

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the Mariconti reference teach or suggest that, because of the existence of another group of E2F proteins in *Arabidopsis thaliana*, Applicants' claimed invention (which makes use of wheat DP proteins) would not function in plants, or would require undue experimentation to work in plants. The Mariconti reference does not teach or suggest that Applicants' claimed methods would not work in plant cells that also express such additional group of E2F proteins.

The Office Action dated March 15, 2005 also asserts that the invention is not enabled because "methods for inhibiting the expression of endogenous genes using antisense technology are unpredictable, since the ability of an antisense DNA sequence to inhibit gene expression is dependent on the specific structure of the DNA sequence and its target" (see, page 14 of the Office Action). The Office Action dated March 15, 2005 cites three references which purportedly supports the Examiner's position. Applicants again disagree.

None of the references cited in the Office Action dated March 15, 2005 teach or suggest that any amount of undue experimentation must be performed to practice the claimed invention. Rather, according to the Office Action dated March 15, 2005, the three references report that some antisense compounds are better than others and that a high degree of sequence homology (i.e., greater than 75%) between the endogenous gene and the antisense compound is required in order for the antisense compound to be effective. The fact that some antisense compounds work better than others is not surprising, let alone sufficient to establish that undue experimentation is required to practice Applicants' claimed invention. In addition, the fact that a high degree of complementarity is also involved is also wholly unsurprising. It does not take any amount of undue experimentation to design an antisense compound with a sufficient degree of complementarity so as to effectuate hybridization. The general principals of the construction of antisense sequences and how to express them in plants is broadly appreciated in the art. Further reference is made to U.S. Patent No. 5,107,065 (cited in the current application and included therein by reference – see page 15, lines 20-27 of the specification) which teaches general principals of the construction of antisense compounds. These are reduced to practice by simple matching to the disclosed sequence. There is no undue burden on the ordinarily skilled artisan given the level of skill in this area and the availability of modern screening practices.

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Thus, there is no reason to believe that one skilled in the art would be required to perform any amount of undue experimentation to make and use the claimed invention. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

**V. The Claims Are Clear And Definite**

Claims 1, 5, 6, 12, 22, and 47 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Although Applicants believe the claims are clear and definite as originally drafted, solely to advance prosecution of the present application, Applicants have amended claims 1, 5, 12, 22, and 47 to be even more clear and definite. No new matter has been added. The claims have not been narrowed.

**A. Claim 1**

The Final Rejection asserts that claim 1 is indefinite in recitation of "controlling." Claim 1 recites a "method of controlling one or more of plant growth, gene expression, cellular DNA replication, cell cycle progression, differentiation and development..." The Office Action dated March 15, 2005 asserts that it is unclear "how" plant growth, gene expression, cellular DNA replication, cell cycle progression, differentiation and development is controlled. The question of "how" these features are controlled, however, is irrelevant. Persons of ordinary skill would have no difficulty in determining whether plant growth, gene expression, cellular DNA replication, cell cycle progression, differentiation and development were controlled by carrying out the claimed method. Accordingly, the claims are definite within the meaning of §112. *In re Mercier*, 185 U.S.P.Q. 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one skilled in the art can determine what subject matter is or is not within the scope of the claims).

The Final Rejection mistakenly asserts that since the recited characteristics (i.e., plant growth, gene expression, cellular DNA replication, cell cycle progression, differentiation and development) can be controlled in many different ways, persons of ordinary skill in the art would not know which aspect of plant growth, gene expression, cellular DNA replication, cell cycle

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progression, differentiation and development to evaluate in order to determine which subject matter is within the scope of the claims. The Examiner, however, provides no evidence or even reasoning that supports the conclusion that persons of ordinary skill would be unable to determine whether plant growth, gene expression, cellular DNA replication, cell cycle progression, differentiation and development were controlled by carrying out the claimed method, even if these characteristics can be controlled in many ways (although such "many ways" have not even been explained by the Examiner).

The Final Rejection also asserts that the phrase "increasing or decreasing" E2F-dimerization partner (DP) protein activity in claim 1 is unclear. The phrase, however, is as clear as can be. One skilled in the art would be able to determine whether it "increases" or whether it "decreases." The Final Rejection asserts that it is unclear how a single method could both increase and decrease DP protein activity or E2F activity. Whether or not the **method** leads to an increase or decrease in DP protein or E2F activity is not the issue, since the method can be carried out using any number of nucleic acid molecules to transform the plant cell (some nucleic acid compounds may lead to an increase in DP protein or E2F activity, whereas other nucleic acid compounds may lead to a decrease in DP protein or E2F activity). The method should not be thought of as a "single" method since it can be carried out with more than one nucleic acid compound. Solely to advance prosecution, however, this phrase has been deleted.

The Final Rejection also asserts that the phrase "increase or decrease" E2F activity in claim 1 is unclear. The phrase, however, is as clear as can be. One skilled in the art would be able to determine whether it "increases" or whether it "decreases." The Final Rejection asserts that it is unclear how a single method could both increase and decrease E2F activity. Whether or not the **method** leads to an increase or decrease in E2F activity is not the issue, since the method can be carried out using any number of nucleic acid molecules to transform the plant cell (some nucleic acid compounds may lead to an increase in E2F activity, whereas other nucleic acid compounds may lead to a decrease in E2F activity). The method should not be thought of as a "single" method since it can be carried out with more than one nucleic acid compound.

The Final Rejection asserts that the phrases "the DNA binding domain", "the heterodimerization domain", and "the nuclear localization signal" are indefinite because there is

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no antecedent basis. Although Applicants believe the claim is clear and definite as written, solely to advance prosecution of the present application, claim 1 has been amended to replace "the" with "a." No change in claim scope is intended.

The Final Rejection asserts that the phrase "E2F-dimerization partner (DP) protein activity" is indefinite because it is allegedly unclear what specific type of activity is increased or decreased. Although Applicants disagree, solely to advance prosecution, this phrase has been deleted from the claim.

**B. Claim 5**

The Final Rejection asserts that the phrase "the plant DP protein level" lacks antecedent support. A plant's "DP protein level", however, is an inherent feature of the plant and, thus, no antecedent basis is explicitly required. The Final Rejection incorrectly asserts, however, that neither claim 1 nor claim 5 require the use of a plant. In fact, claim 5 recites "The method of Claim 1 wherein transformation of the plant cell with said nucleic acid results in altering the plant DP protein level." To be even more clear, Applicants have amended claim 5 to delete "plant." There is no change in claim scope.

The phrases "altering the DP protein level", "altering E2F-DP transactivation properties", and "modulation of E2F-DP DNA-binding activity" with respect to the terms "altering" and "modulation" do not lack clarity. Alteration in the level of a protein or E2F-DP transactivation properties or modulation of E2F-DP DNA-binding activity can only be in the sense of increasing or decreasing. As discussed above, the claimed methods are not limited to the employment of a single nucleic acid molecule. Thus, in some methods, depending upon the particular nucleic acid molecule employed in the method, the DP protein level or E2F-DP transactivation properties or E2F-DP DNA-binding activity may be altered or modulated so as to increase DP protein level or E2F-DP transactivation properties or E2F-DP DNA-binding activity. In other embodiments, the DP protein level or E2F-DP transactivation properties or E2F-DP DNA-binding activity may be altered so as to decrease DP protein level or E2F-DP transactivation properties or E2F-DP DNA-binding activity.

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The phrase "increasing or decreasing" in regard to the binding of DP to E2F is not indefinite. As stated above, the claimed method cannot be regarded as a single method limited to transformation with a single nucleic acid molecule. Indeed, the method can be employed with any number of nucleic acid molecules. Thus, in some methods, depending upon the particular nucleic acid molecule employed in the method, binding of DP to E2F may increase. In other embodiments, binding of DP to E2F may decrease.

**C. Claim 6**

Claim 6 recites a method wherein the "DP protein activity is increased or decreased alone and/or in combination with a modification of the levels or activity of plant E2F and/or plant Rb." The Final Rejection asserts that the terms "modification" and "activity" are indefinite. The phrase "modification of the levels or activity of plant E2F and/or plant Rb" is broadly drafted to include any modification of the levels or activity of plant E2F or plant Rb. The term is broad but not unclear. Indeed, "modification" of levels or activity of plant E2F and/or plant Rb again means an increase or decrease in the level or activity of plant E2F and/or plant Rb.

Recitation of "increased or decreased" in claim 6 is also alleged to render the claim indefinite. The phrase "increasing or decreasing" in regard to the DP protein activity is not indefinite. As stated above, the claimed method cannot be regarded as a single method limited to transformation with a single nucleic acid molecule. Indeed, the method can be employed with any number of nucleic acid molecules. Thus, in some methods, depending upon the particular nucleic acid molecule employed in the method, DP protein activity may increase. In other embodiments, DP protein activity may decrease.

**D. Claim 12**

The phrases "ability to" and "increase or decreases" have been removed from the claims.

The Final Rejection asserts that the term "modulate" renders the claim indefinite. Again, as stated throughout the present response, one skilled in the art would understand that the term "modulate" means increases or decreases.

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The Final Rejection asserts that the phrases "the DNA binding domain", "the heterodimerization domain", and "the nuclear localization signal" are indefinite because there is no antecedent basis. Although Applicants believe the claim is clear and definite as written, solely to advance prosecution of the present application, claim 12 has been amended to replace "the" with "a." No change in claim scope is intended.

**E. Claim 22**

Although Applicants disagree with the reasons set forth in the Final Rejection, the phrases "ability to", "modulate E2F binding", and "increases or decreases" have been removed from claim 22 for the purposes of clarity.

The Final Rejection asserts that the phrases "the DNA binding domain", "the heterodimerization domain", and "the nuclear localization signal" are indefinite because there is no antecedent basis. Although Applicants believe the claim is clear and definite as written, solely to advance prosecution of the present application, claim 22 has been amended to replace "the" with "a." No change in claim scope is intended.

**F. Claim 47**

Although Applicants disagree with the reasons set forth in the Final Rejection, the phrases "modulation", "or effect thereof", and "increases or decreases" have been removed from claim 47 for the purposes of clarity.

The Final Rejection asserts that the phrases "the DNA binding domain", "the heterodimerization domain", and "the nuclear localization signal" are indefinite because there is no antecedent basis. Although Applicants believe the claim is clear and definite as written, solely to advance prosecution of the present application, claim 47 has been amended to replace "the" with "a." No change in claim scope is intended.

In view of the foregoing, the claims are clear and definite. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

**DOCKET NO.: BTG0004-100 (141183US01)****PATENT****VI. Conclusion**

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 665-6914 if there are any questions regarding Applicants' claimed invention.

Respectfully submitted,

  
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Date: 7 March 2006

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